IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:
Serial No.:
Filing Date:
For:

Docket No.:
Group Art Unit:
Examiner:

DECLARATION OF SHERMAN FONG, Ph.D. UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Sherman Fong, Ph.D. declare and say as follows: -

1. I am an inventor of the above-identified patent application.

2. I was awarded a Ph.D. in Microbiology by the University of California at Davis, CA in 1975.

3. After postdoctoral training and holding various research positions at Scripps Clinic and Research Foundation, La Jolla, CA, I joined Genentech, Inc., South San Francisco, CA in 1987. I am currently a Senior Scientist at the Department of Immunology/Discovery Research of Genentech, Inc.

4. My scientific Curriculum Vitae is attached to and forms part of this Declaration.

5. I am familiar with the skin vascular permeability assay (Assay #64), which has been used by me and others under my supervision, to test the activities of novel polypeptides discovered in Genentech's Secreted Protein Discovery Initiative project.

6. The skin vascular permeability assay, is also known in the art as the Miles assay and was first described by Miles and Miles in 1952 when they studied vascular responses to histamine (Miles A.A., and Miles E.M., J. Physiol., 1952, 118: 228-257, see **Exhibit A**). Since then it has been reliably used for identifying proinflammatory molecules.

7. Proinflammatory molecules can directly or indirectly cause vascular permeability by causing immune cells to exit from the blood stream and move to the site of injury or infection. These proinflammatory molecules recruit cells like leukocytes which includes monocytes, macrophages,

basophils, and eosinophils. These cells secrete a range of cytokines which further recruit and activate other inflammatory cells to the site of injury or infection. How leukocytes exit the vasculature and move to their appropriate destination of injury or infection is critical and is tightly regulated. Leukocytes move from the blood vessel to injured or inflamed tissues by rolling along the endothelial cells of the blood vessel wall and then extravasate through the vessel wall and into the tissues (see **Exhibit B**). This diapedesis and extravasation step involves cell activation and a stable leukocyte-endothelial cell interaction

8. Hence, proinflammatory molecules are useful in treating infections, as local administration of the proinflammatory polypeptide would stimulate immune cells already present at the site of infection and induce more immune cells to migrate to the site, thus removing the infection at a faster rate. Examples of proinflammatory molecules that induce neutrophils to extravasate are MIP-1 and MIP-2. Other proinflammatory may be able to activate immune cells, as shown with the CXC chemokines activation of neutrophils, and the non-CXC chemokines which are chemotactic for T lymphocytes (Baggiolini *et al.*, Adv Immunology 1994; 55 97-179 see **Exhibit C**).

Inappropriate expression of proinflammatory molecules may cause an abnormal immune cell reponse and lead tissue destruction. Examples of such abnormal immune reponses include at least the following conditions: psoriasis, inflammatory bowel disease, renal disease, arthritis, immune-mediated alopecia, stroke, encephalitis, Multiple Sclerosis, hepatitis, and others. Therefore, inhibitors of such proinflammatory molecules find use in the treatment of these conditions. Further, proinflammatory molecules with angiostatic properties are useful in the inhibition of angiogenesis during abnormal wound healing or abnormal inflammation during infection. Further, proinflammatory molecules that are also angiostatic are useful in treating tumors, by inhibiting the neovascularization that accompanies tumor growth (Strieter RM. *et al.*, J. Biol. Chem. 1995; 270: 27348-27357 see **Exhibit D**). Administration of the proinflammatory polypeptide, either alone or in combination with another angiostatic factor such as anti-VEGF, would be useful for limiting or reducing tumor growth.

9. The Skin Vascular Permeability Assay was used to identify such proinflammatory and immune related molecules. Miles and Miles described this assay initially in 1952, in their work on vascular response to histamine (Miles A.A., and Miles E.M., J. Physiol. 1952; (118) 228-257 *supra*). Miles and Miles solved the critical variables in the assay, such as performing the intradermal injection, where to inject, effects of temperature, effects of dosage, and effects of anesthetic used. Using this assay, Miles and Miles proved that histamine increased the capillary permeability in the skin, thus allowing cells to exit the vasculature. The assay was used qualitatively until other investigators quantitated it by

extracting the amount of accumulated marker dye and measuring its absorbance at 620 nm (Udaka et al., Proc Soc Exp Biol Med 1970; (133) 1384-1387 see **Exhibit E**).

10. The Skin Vascular permeability assay was used in the clinic in determining if blood coagulation factor XIII (FXIII) could be used in treating Shonlein Henoch Purpura (SHP) (Hirahara K., et al., Thrombosis Res 1993; 71(2) 139-148 see **Exhibit F**). SHP is an immunovascular disease, characterized by hemorrhagic skin lesions, gastro-intestinal bleeding and hematuria. The physiology of SHP was undetermined, but destruction of FXIII by leukocytes that migrated into the area and secreted destructive proteases was believed to play a role. This hypothesis was tested by using antibodies raised to guinea pig endothelial cells. These antibodies were specific for endothelial cells and not for fibroblasts, and when injected into the skin of a guinea pig, caused increased vascular permeability. When FXIII was mixed with this antibody and injected, the marker dye showed less spreading, indicating that FXIII was suppressing the vascular permeability and did so in a dose dependant manner. The conclusion was that FXIII was stabilizing the microvasculature, leading to less permeability, and therefore FXIII may be useful in the treatment of SHP.

11. The Skin Vascular Permeability assay has been confirmed by alternate experimental methods. Senger et al., used the Skin Vascular Permeability assay as described by Miles and determined that a secreted factor they called VPF (later determined to be VEGF), caused vascular permeability (Senger D.R., et al., Science 1983; (219) 983-985 see **Exhibit G**). In these experiments VPF was subjected to the Skin Vascular Permeability assay, the sites of injection were analyzed by light and electron microscopy and VPF caused vascular permeability without damaging endothelial cells or causing mast cell degranulation.

12. Yeo et al., confirmed the viability of the Skin Vascular Permeability assay by correlating it with disassociation enhanced lanthanide fluoroimmunoassay (DELFIA) results (Yeo K.T., Clin. Chem 1992; (38) 71-75 see **Exhibit H**). VPF (VEGF) was first measured using the Skin Vascular Permeability assay by quantifiying the amount of accumulated dye in the skin as described in Udaka et al., (supra). Anti-VPF antibodies were used to quantitate the amount of VPF in the DELFIA. This assay has increased sensitivity as the result is read by a fluorometer, instead of dye absorbance. The investigators found that the sensitivity of the DELFIA was greater than the Skin Vascular Permeability assay, but there was an excellent linear correlation ($r^2 = 0.94$) between the two assays.

13. The Applicant's Skin Vascular Permeability assay was conducted using anesthetized Hairless guinea pigs. A sample of a purified PRO polypeptide or a conditioned media test sample was injected intradermally onto the backs of the test animals with 100 µL per injection site. It was possible to have up to about 24 injection sites per animal. One mL of Evans Blue dye (1% in physiologic buffered saline), was injected intracardially as the marker dye. Blemishes at the injection sites were then measured (mm diameter) after 1 hr, 6 hrs and 24 hrs post injection. Animals were sacrificed at the appropriate time after injection, and each skin injection site was biopsied and fixed in paraformaldehyde. The biopsies were then prepared for histopathalogic evaluation. Each site was evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation were scored as positive. Polypeptides tested stimulated an immune response and induced mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal. Perivascular infiltrate at the injection site was scored as positive; no infiltrate at the site of injection is scored as negative.

An example of a positive reaction is shown in **Exhibit I**. The top row is injected with Interleukin-8 (IL-8) control and shows no increased vascular permeability. The 2nd row from the top is VEGF as a positive control. The 2 bottom rows show a positive result from a PRO polypeptide, performed in duplicate.

14. It is my opinion that the PRO polypeptide that shows activity in the Skin Vascular permeability assay has specific, substantial and credible utilities. In the experiments performed in the instant application, the results of the skin vascular permeability assay were further analyzed by histopathological examination to rule out inflammation due to endothelial cell damage or mast cell degranulation. Hence, the vascular permeability observed was not due to histamine release or endothelial cell damage. Examples of utilities include, enhancing immune cell recruitment to sites of injury or infection, or inhibitors to treat autoimmune diseases such as psoriasis etc. as discussed above. Furthermore, the angiogenic or angiostatic properties of proinflammatory molecules would also find practical utility in controlling tumorigenesis.

15. I declare further that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true and further, that these statements are made with the knowledge that willful statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent granted thereon.

Date: 8/27/04

By: Sherman Fong
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Education:

1978 - 1980 Postdoctoral Fellow in Immunology, Research Institute of Scripps Clinic, Scripps Clinic and Research Foundation, La Jolla, California

1975 - 1978 Postdoctoral Fellow in Immunology, University of California at San Francisco, San Franciso, California

1970 - 1975 Ph.D. in Microbiology, University of California at Davis, California

1966 - 1970 B.A. in Biology/Microbiology, San Francisco State University, San Francisco, California

Professional Positions:
Currently: Senior Scientist, Department of Immunology/Discovery Research, Genentech, Inc., South San Francisco, California

8/00-8/01 Acting Director, Department of Immunology, Genentech, Inc. South San Francisco, California

10/89 Senior Scientist in the Department of Immunology/Discovery Research, Genentech, Inc. South San Francisco, California

3/89 - 10/89 Senior Scientist and Immunobiology Group Leader, Department of Pharmacological Sciences, Immunobiology Section/Medical Research and Development, Genentech, Inc., S. San Francisco, California

9/87 - 3/89 Scientist, Department of Pharmacological Sciences, Immunopharmacology Section/Medical Research and Development, Genentech, Inc., S. San Francisco, California

1/82 - 9/87 Assistant Member (eq. Assistant Professor level), Department of Basic and Clinical Research, Division of Clinical Immunology, Scripps Clinic and Research Foundation, La Jolla, California

6/80 - 12/81 Scientific Associate in the Department of Clinical Research, Division of Clinical Immunology, Scripps Clinic and Research Foundation, La Jolla, California

7/78 - 6/80 Postdoctoral training in the laboratory of Dr. J. H. Vaughan, Chairman, Department of Clinical Research, Division of Clinical Immunology, Scripps Clinic and Research Foundation, La Jolla, California

2/75 - 6/78 Postdoctoral training in the laboratory of Dr. J. W. Goodman, Department of Microbiology and Immunology, School of Medicine, University of California, San Francisco, California

7/71 - 12/74 Research Assistant and Graduate Student, Department of Medical Microbiology, School of Medicine, University of California, Davis, California, under Dr. E. Benjamini

Awards:
Recipient: National Institutes of Health Postdoctoral Fellowship Award (1975).

Recipient: Special Research Award, (New Investigator Award), National Institute of Health (1980).

Recipient: P.I., Research Grant Award, National Institute of Health (1984).

Recipient: Research Career Development Award (R01), National Institutes of Health (1985).

Recipient: P.I., Multi-Purpose Arthritis Center Resarch Grant, NIH (1985)

Recipient: P.I., Resarch Grant Award, (R01 Renewal), National Institute of Health (1987).

Scientific Associations:

Sigma Xi, University of California, Davis, California Chapter

Member, The American Association of Immunologists

Committee Service and Professional Activities:

Member of the Immunological Sciences Study Section, National Institutes of Health Research Grant Review Commitee, (1988-1992).

Advisory Committee, Scientific Review Committee for Veteran's Administration High Priority Program on Aging, 1983.

Ad Hoc member of Immunological Sciences Study Section, National Institutes of Health, 1988.

Ad Hoc Reviewer: Journal of Clinical Investigations, Journal of Immunology, Arthritis and Rheumatism, International Immunology, Molecular Cell Biology, and Gastroenterology

Biotechnology Experience

Established at Genentech in 1987-1989 within the Immunobiology Laboratory, in the Department of Pharmcological Sciences, group to study the immunogenicity of recombinant hGH (Protropin®) in hGH transgenic mice.

Served as Immunologist on the **Biochemical Subteam for Protropin® Project** team.

Served as Immunologist on the **Met-less hGH and Dnase project teams**, two FDA approved biological drugs: second generation hGH Nutropin® and Pulmozyme® (DNase).

Served immunologist in1989-1990 on the **CD4-IgG project team** carrying out in vitro immunopharmacological studies of the effects of CD4-IgG on the in vitro human immune responses to mitogens and antigens and on neutrophil responses in support of the filing of IND to FDA in 1990 for use of CD4-IgG in the prevention of HIV infection. Product was dropped.

In 1989-1991, initiated and carried research and development work on antibodies to CD11b and CD18 chains of the leukocyte β2 integrins. Provided preclinical scientific data to **Anti-CD18 project team**

supporting the advancement of humanized anti-CD18 antibody as anti-inflammatory in the acute setting. IND filed in 1996 and currently under clinical evaluation.

1993-1997, **Research Project Team leader** for small molecule $\alpha 4\beta 1$ integrin antagonist project. Leader for collaborative multidisciplinary team (N=11) composed of immunologists, molecular/cell biologists, protein engineers, pathologists, medicinal chemists, pharmacologists, pharmaceutical chemists, and clinical scientists targeting immune-mediated chronic inflammatory diseases. Responsible for research project plans and execution of strategy to identify lead molecules, assessment of biological activities, preclinical evaluation in experimental animals, and identification of potential clinical targets. Responsible for identification, hiring, and working with outside scientific consultants for project. Helped established and responsible for maintaining current research collaboration with Roche-Nutley. Project transfered to Roche-Nutley.

1998-present, worked with Business Development to identify and create joint development opportunity with LeukoSite (currently Millennium) for monoclonal antibody against $\alpha 4\beta 7$ intergin (LDP-02) for therapeutic treatment for inflammatory bowel disease (UC and Crohn';s disease). Currently, working as scientific advisor to the core team for phase II clinical trials for LDP-02.

Currently, **Research Project Team Biology Leader** (1996-present) for small molecule antagonists for $\alpha 4\beta 7$/MAdCAM-1 targeting the treatment of human inflammatory bowel diseases and diseases of the gastrointestinal tract. Responsible for leading collaborative team (N=12) from Departments of Immunology, Pathology, Analytical Technology, Antibody Technology, and Bio-Organic Chemistry to identify and evaluate lead drug candidates for the treatment of gastrointestinal inflammatory diseases.

Served for nearly fifteen years as **Ad Hoc reveiwer** on Genentech Internal Research Review Committee, Product Development Review Committee, and Pharmacological Sciences Review Committee.

Worked as Scientific advisor with staff of the **Business Development** Office on numerous occasions at Genentech, Inc. to evaluate the science of potential in-licensing of novel technologies and products.

2000-2001 Served as Research Discovery representative on Genentech Therapeutic Area Teams (Immunology/Endocrine, Pulmonary/Respiratory Disease Task Force)

Invited Symposium Lectures:

Session Chairperson and speaker, American Aging Association 12th Annual National Meeting, San Francisco, California, 1982.

Invited Lecturer, International Symposium, Mediators of Immune Regulation and Immunotherapy, University of Western Ontario, London, Ontario, Canada, 1985.

Invited Lecturer, workshop on Human IgG Subclasses, Rheumatoid Factors, and Complement. American Association of Clinical Chemistry, San Francisco, California, 1987.

Plenary Lecturer, First International Waaler Conference on Rheumatoid Factors, Bergen, Norway, 1987.

Invited Lecturer, Course in Immunorheumatology at the Universite aux Marseilles, Marseilles, France, 1988.

Plenary Lecturer, 5th Mediterranean Congress of Rheumatology, Istanbul, Turkey, 1988.

Invited Lecturer, Second Annual meeting of the Society of Chinese Bioscientist of America, University of California, Berkeley, California, 1988.

Lecturer at the inaugural meeting of the Immunology by the Bay sponsored by The Bay Area Bioscience Center. The β2 Integrins in Acute Inflammation, July 14, 1992.

Lecturer, "Research and Development -- An Anatomy of a Biotechnology Company", University of California, Berkeley, Extension Course, given twice a year--March 9, 1995 to June 24, 1997.

Lecturer, "The Drug Development Process – Biologic Research - Genomics", University of California, Berkeley Extension, April 21, 1999, October, 1999, April 2000, October, 2000.

Lecturer, "The Drug Development Process – Future Trends/Impact of Pharmacogenomics", University of California Berkeley Extension, April 2001, October 2001, April 2002.

Invited Speaker, "Targeting of Lymphocyte Integrin α4β7 Attentuates Inflammatory Bowel Diseases", in Sympoium on "Nutrient effects on Gene Expression" at the Institute of Food Technology Symposium, June, 2002.

Patents:

Dennis A. Carson, Sherman Fong, Pojen P. Chen.
U.S. Patent Number 5,068,177: Anti-idiotype Antibodies induced by Synthetic Polypeptides, Nov. 26, 1991

Sherman Fong, Caroline A. Hebert, Kyung Jin Kim and Steven R. Leong.
U.S. Patent Number 5,677,426: Anti-IL-8 Antibody Fragments, Oct. 14, 1997

Claire M. Doerschuk, Sherman Fong, Caroline A. Hebert, Kyung Jin Kim, Steven R. Leong. U.S. Patent Number 5,686,070: Methods for Treating Bacterial Pneumonia, Nov. 11, 1997

Claire M. Doerschuk, Sherman Fong, Caroline A. Hebert, Kyung Jin Kim, Steven R. Leong. U.S. Patent 5,702,946: Anti-IL-8 Monoclonal Antibodies for the Treatment of Inflammatory Disorders, Dec. 30, 1997

Sherman Fong, Caroline A. Hebert, Kyung Jin Kim, Steven R. Leong.
U.S. Patent Number 5,707,622: Methods for Treating Ulcerative Colits, Jan. 13, 1998

Sherman Fong, Napoleone Ferrara, Audrey Goddard, Paul Godowski, Austin Gurney, Kenneth Hillan, and Mickey Williams. U.S. Patent Number 6,074,873: Nucleic acids encoding NL-3, June 13, 2000

Sherman Fong, Napoleone Ferrara, Audrey Goddard, Paul Godowski, Austin Gurney, Kenneth Hillan, and Mickey Williams. U.S. Patent Number 6,348,351 B1: The Receptor Tyrosine Kinase Ligand Homologues. February 19, 2002

Patent Applications:

Sherman Fong, Kenneth Hillan, Toni Klassen
U.S. Patent Application: "Diagnosis and Treatment of Hepatic Disorders"

Sherman Fong, Audrey Goddard, Austin Gurney, Daniel Tumas, William Wood
U.S. Patent Application: Compositions and Methods for the Treatment of Immune Related Diseases.

Sherman Fong, Mary Gerritsen, Audrey Goddard, Austin Gurney, Kenneth Hillan, Mickey Williams, William Wood . U.S. Patent Application: Promotion or Inhibition of Cardiovasculogenesis and Angiogenesis

Avi Ashkenazi, Sherman Fong, Audrey Goddard, Austin Gurney, Mary Napier, Daniel Tumas, William Wood. US Patent Application: Compounds, Compositions and Methods for the Treatment of Diseases Characterized by A33-Related Antigens

Chen, Filvaroff, Fong, Goddard, Godowski, Grimaldi, Gurney, Hillan, Tumas, Vandlen, Van Lookeren, Watanabe, Williams, Wood, Yansura
US Patent Application: IL-17 Homologous Polypeptides and Therapeutic Uses Thereof

Ashkenazi, Botstein, Desnoyers, Eaton, Ferrara, Filvaroff, Fong, Gao, Gerber, Gerritsen, Goddard, Godowski, Grimaldi, Gurney, Hillan, Kljavin, Mather, Pan, Paoni, Roy, Stewart, Tumas, Williams, Wood
US Patent Application: Secreted And Transmembrane Polypeptides And Nucleic Acids Encoding The Same

Publications:

1. Scibienski R, Fong S, Benjamini E: Cross tolerance between serologically non-cross reacting forms of egg white lysozyme. J Exp Med 136:1308-1312, 1972.

2. Scibienski R, Harris M, Fong S, Benjamini E: Active and inactive states of immunological unresponsiveness. J Immunol 113:45-50, 1974.

3. Fong S: Studies on the relationship between the immune response and tumor growth. Ph D Thesis, 1975.

4. Benjamini E, Theilen G, Torten M, Fong S, Crow S, Henness AM: Tumor vaccines for immunotherapy of canine lymphosarcoma. Ann NY Acad Sci 277:305, 1976.

5. Benjamini E, Fong S, Erickson C, Leung CY, Rennick D, Scibienski RJ: Immunity to lymphoid tumors induced in syngeneic mice by immunization with mitomycin C treated cells. J Immunol 118:685-693, 1977.

6. Goodman JW, Fong S, Lewis GK, Kamin R, Nitecki DE, Der Balian G: T lymphocyte activation by immunogenic determinants. Adv Exp Biol Med 98:143, 1978.

7. Goodman JW, Fong S, Lewis GK, Kamin R, Nitecki DE, Der Balian G: Antigen structure and lymphocyte activation. Immunol Rev 39:36, 1978.

8. Fong S, Nitecki DE, Cook RM, Goodman JW: Spatial requirements of haptenic and carrier determinants for T-dependent antibody responses. J Exp Med 148:817, 1978.

9. Fong S, Chen PP, Nitecki DE, Goodman JW: Macrophage-T cell interaction mediated by immunogenic and nonimmunogenic forms of a monofunctional antigen. Mol Cell Biochem 25:131, 1979.

10. Tsoukas CD, Carson DA, Fong S, Pasquali J-L, Vaughan JH: Cellular requirements for pokeweed mitogen induced autoantibody production in rheumatoid arthritis. J Immunol 125:1125-1129, 1980.

11. Pasquali J-L, Fong S, Tsoukas CD, Vaughan JH, Carson DA: Inheritance of IgM rheumatoid factor idiotypes. J Clin Invest 66:863-866, 1980.

12. Fong S, Pasquali J-L, Tsoukas CD, Vaughan JH, Carson DA: Age-related restriction of the light chain heterogeneity of anti-IgG antibodies induced by Epstein-Barr virus stimulation of human lymphocytes in vitro. Clin Immunol Immunopathol 18:344, 1981.

13. Fong S, Tsoukas CD, Frincke LA, Lawrance SK, Holbrook TL, Vaughan JH, Carson DA: Age-associated changes in Epstein-Barr virus induced human lymphocyte autoantibody responses. J Immunol 126:910-914, 1981.

14. Tsoukas CD, Fox RI, Slovin SF, Carson DA, Pellegrino M, Fong S, Pasquali J-L, Ferrone S, Kung P, Vaughan JH: T lymphocyte-mediated cytotoxicity against autologous EBV-genome-bearing B cells. J Immunol 126:1742-1746, 1981.

15. Fong S, Tsoukas CD, Pasquali J-L, Fox RI, Rose JE, Raiklen D, Carson DA, Vaughan JH: Fractionation of human lymphocyte subpopulations on immunoglobulin coated petri dishes. J Immunol Methods 44:171-182, 1981.

16. Pasquali J-L, Tsoukas CD, Fong S, Carson DA, Vaughan JH: Effect of Levamisole on pokeweed mitogen stimulation of immunoglobulin production in vitro. Immunopharmacology 3:289-298, 1981.

17. Pasquali J-L, Fong S, Tsoukas CD, Hench PK, Vaughan JH, Carson DA: Selective lymphocyte deficiency in seronegative rheumatoid arthritis. Arthritis Rheum 24:770-773, 1981.

18. Fong S, Fox RI, Rose JE, Liu J, Tsoukas CD, Carson DA, Vaughan JH: Solid- phase selection of human T lymphocyte subpopulations using monoclonal antibodies. J Immunol Methods 46:153-163, 1981.

19. Pasquali J-L, Fong S, Tsoukas CD, Slovin SF, Vaughan JH, Carson DA: Different populations of rheumatoid factor idiotypes induced by two polyclonal B cell activators, pokeweed mitogen and Epstein-Barr virus. Clin Immunol Immunopathol 21:184-189, 1981.

20. Carson DA, Pasquali J-L, Tsoukas CD, Fong S, Slovin SF, Lawrance SK, Slaughter L, Vaughan JH: Physiology and pathology of rheumatoid factors. Springer Semin Immunopathol 4:161-179, 1981.

21. Fox RI, Fong S, Sabharwal N, Carstens SA, Kung PC, Vaughan JH: Synovial fluid lymphocytes differ from peripheral blood lymphocytes in patients with rheumatoid arthritis. J Immunol 128:351-354, 1982.

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23. Tsoukas CD, Fox RI, Carson DA, Fong S, Vaughan JH: Molecular interactions in human T-cell-mediated cytotoxicity to Epstein-Barr virus. I. Blocking of effector cell function by monoclonal antibody OKT3. Cell Immunol 69:113-121, 1982.

24. Sabharwal UK, Vaughan JH, Fong S, Bennett P, Carson DA, Curd JG: Activation of the classical pathway of complement by rheumatoid factors: Assessment by radioimmunoassay for C4. Arthritis Rheum 25:161-167, 1982.

25. Fox RI, Carstens SA, Fong S, Robinson CA, Howell F, Vaughan JH: Use of monoclonal antibodies to analyze peripheral blood and salivary gland lymphocyte subsets in Sjogren's Syndrome. Arthritis Rheum 25:419, 1982.

26. Fong S, Miller JJIII, Moore TL, Tsoukas CD, Vaughan JH, Carson DA: Frequencies of Epstein-Barr virus inducible IgM anti-IgG B lymphocytes in normal children and in children with Juvenile Rheumatoid Arthritis. Arthritis Rheum 25:959-965, 1982.

27. Goodman JW, Nitecki DE, Fong S, Kaymakcalan Z: Antigen bridging in the interaction of T helper cells and B cells. Adv Exp Med Biol 150:219-225, 1982.

28. Goodman JW, Nitecki DE, Fong S, Kaymakcalan Z: Antigen bridging in T cell-B cell interaction: Facts or fiction. In: Protein Conformation as Immunologic Signal. EMBO Workshop, Portonenere, Italy, 1982.

29. Tsoukas CD, Carson DA, Fong S, Slovin SF, Fox RI, Vaughan JH: Lysis of autologous Epstein-Barr virus infected B cells by cytotoxic T lymphocytes of rheumatoid arthritis patients. Clin Immunol Immunopathol 24:8-14, 1982.

30. Fong S, Vaughan JH, Tsoukas CD, Carson DA: Selective induction of autoantibody secretion in human bone marrow by Epstein-Barr virus. J Immunol 129:1941-1945, 1982.

31. Sabharwal UK, Fong S, Hoch S, Cook RD, Vaughan JH, Curd JG: Complement activation by antibodies to Sm in systemic lupus erythematosus. Clin Exp Immunol 51:317-324, 1983.

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33. Welch MJ, Fong S, Vaughan JH, Carson DA: Increased frequency of rheumatoid factor precursor B lymphocytes after immunization of normal adults with tetanus toxoid. Clin Exp Immunol 51:299-305, 1983.

34. Fong S, Vaughan JH, Carson DA: Two different rheumatoid-factor producing cell populations distinguished by the mouse erythrocyte receptor and responsiveness to polyclonal B cell activators. J Immunol 130:162-164, 1983.

35. Fox RI, Hueniken M, Fong S, Behar S, Royston I, Singhal SK, Thompson L: A novel cell surface antigen (T305) found in increased frequency on acute leukemia cells and in autoimmune disease states. J Immunol 131:762-767, 1983.

36. Fong S: Solid-phase panning for the fractionation of lymphoid cells. In: Cell separation: methods and selected applications. Pretlow TG, Pretlow TP (eds.) pp. 203-219. Academic Press, New York, 1983.

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38. Fong S, Gilbertson TA, Carson DA: The internal image of IgG in cross- reactive anti-idiotypic antibodies against human rheumatoid factors. J Immunol 131:719-724, 1983.

39. Fox RI, Adamson TC, Fong S, Young C, Howell FV: Characterization of the phenotype and function of lymphocytes infiltrating the salivary gland in patients with primary Sjogren syndrome. Diagn Immunol 1:233-239, 1983.

40. Fox RI, Adamson III TC, Fong S, Robinson CA, Morgan EL, Robb JA, Howell FV: Lymphocyte phenotype and function in pseudolymphoma associated with Sjogren's syndrome. J Clin Invest 72:52-62, 1983.

41. Fong S, Gilbertson TA, Chen PP, Vaughan JH, Carson DA: Modulation of human rheumatoid factor-specific lymphocyte responses with a cross- reactive anti-idiotype bearing the internal image of antigen. J Immunol 132:1183-1189, 1984.

42. Chen PP, Houghten RA, Fong S, Rhodes GH, Gilbertson TA, Vaughan JH, Lerner RA, Carson DA: Anti-hypervariable region antibody induced by a defined peptide. A new approach for studying the structural correlates of idiotypes. Proc Natl Acad Sci USA 81:1784-1788, 1984.

43. Fox RI, Fong S, Tsoukas CD, Vaughan JH: Characterization of recirculating lymphocytes in rheumatoid arthritis patients: Selective deficiency of natural killer cells in thoracic duct lymph. J Immunol 132:2883-2887, 1984.

44. Chen PP, Fong S, Normansell D, Houghten RA, Karras JG, Vaughan JH, Carson DA: Delineation of a cross-reactive idiotype on human autoantibodies with antibody against a synthetic peptide. J Exp Med 159:1502-1511, 1984.

45. Fong S, Carson DA, Vaughan JH: Rheumatoid factor. In: Immunology of Rheumatic Diseases. Gupta S, Talal N (eds.): Chapter 6. pp. 167-196. Plenum Publishing Corp., New York, 1985.

46. Fong S: Immunochemistry. In: Immunology as applied to Otolaryngology. Ryan AF, Poliquis JF, Harris A (eds.): pp. 23-53. College Hill Press, San Diego, 1985.

47. Fong S, Chen PP, Vaughan JH, Carson DA: Origin and age-associated changes in the expression of a physiologic autoantibody. Gerontology 31:236-250, 1985.

48. Chen PP, Fong S, Houghten RA, Carson DA: Characterization of an epibody: An anti-idiotype which reacts with both the idiotype of rheumatoid factors (RF) and the antigen recognized by RFs. J Exp Med 161:323, 1985.

49. Chen PP, Goni F, Fong S, Jirik F, Vaughan JH, Frangione B, Carson DA: The majority of human monoclonal IgM rheumatoid factors express a primary structure-dependent cross-reactive idiotype. J Immunol 134:3281-3285, 1985.

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